UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,479	03/29/2007	Bradley L. Urquhart	10935-35	7049

1059 7590 06/10/2009

BERESKIN AND PARR LLP/S.E.N.C.R.L., s.r.l.
40 KING STREET WEST
BOX 401
TORONTO, ON M5H 3Y2
CANADA

EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,479	URQUHART ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-15* is/are pending in the application.

4a) Of the above claim(s) *2 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/23/2009 has been entered.

Election/Restrictions

2. Based on the arguments with respect to N-Acetylcysteine and the Ventura and Friedman reference arguments considered, the compounds under examination are expanded to include N-Acetylcysteine (NAC), which would be a “derivative” of mesna, based on the sulfhydryl group, and the implication that NAC may be used to establish the predictability or unpredictability of results.

Response to Arguments

3. Applicants' arguments, filed 2/23/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

4. Applicant's arguments with respect to the rejection under 35 USC 103 have been fully considered but they are not persuasive:

Claims 1, 3-5 and 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pendyala, et al. ("Intravenous Ifofamide/Mesna Is Associated with Depletion of Plasma Thiols without Depletion of Leukocyte Glutathione"; 2000; Clinical Cancer Research; 6(4): 1314-1321; cited in a previous Office Action); and Cohen ("Methyl group deficiency and guanidine production in Uremia; 2003 Feb; Molecular and Cellular Biochemistry; 244(1-2): 31-36; cited in a previous Office Action); in view of Wilcox (WO 01/30352 A1; 2001; IDS 8/3/2006 reference).

The rejection is maintained for the reasons of record.

Receipt is acknowledged of the IDS references filed 2/23/2009, which include Friedman et al. ("Te Effect of N-Acetylcysteine on Plasma Total Homocysteine Levels in Hemodialysis: A Randomized, Controlled Study"; 2003 Feb; American Journal of Kidney Diseases; 41(2): 442-446; IDS 2/23/2009 reference 15); Ventura et al. ("urinary and Plasma Homocysteine and Cysteine Levels during Prolonged Oral N-Acetylcysteine Therapy"; 2003 June; Pharmacology; 68(2): 105-114; IDS 2/23/2009 reference 16.

Applicant argues that in view of Friedman and Ventura, considering applicant's arguments of record; the references now provide support for the surprising and unexpected finding described in the present application that Mesna was able to decrease post-dialysis t-Hcy, while it itself is also removed from the plasma during dialysis in patients with ESRD. The demonstration of these findings is not disputed. However, the fact that the demonstrated results is unexpected is not convincing based on Friedman and Ventura. With respect to Friedman and Ventura, applicant previously argued (in the 8/12/2008 Reply, pp. 9-10, bridging paragraph) that in the present

application Mesna is used to exchange with the Hcy on Hcy-cys-34 albumin thereby releasing free Hcy (reduced and mixed disulfide forms), which in patients with normal renal function can be eliminated in the urine; that applicants were able to further show, for the first time that Mesna is removed from its bound form in the plasma and is eliminated by dialysis; that a similar strategy was previously attempted using N-acetylcysteine, however in patients on chronic hemodialysis it was not successful (according to Friedman), which contrasts with a study on healthy subjects where N-acetylcysteine was able to lower tHcy (according to Ventura); that this highlights the surprising and unexpected finding described in the instant application that Mesna was able to decrease post-dialysis t-Hcy while, it itself is also removed from the plasma during dialysis in patients with ESRD.

Consideration of the Ventura reference indicates a tHcy baseline level of 14.1±6.64 in Group A (the no therapy group, initially), which is unchanged at 14.5 or 14.6 with no therapy, but decreases to 12.2±5.98 or 11.6±4.55 upon administration of 1,800 mg NAC (p. 108, Table 2, Group A); in Group B. The 600 mg NAC group (Group B) starts with a tHcy baseline of 12.9±3.98, which drops to 11.6±3.72 (considered slight, but significant, p. 110, 3rd paragraph), a value which further drops to 11.16±3.41 and 10.2 ±1.81 during the T3 and T4 time periods, where 1,800 mg NAC is administered (Table 2). The 1,800 mg group (Group C) starts with a tHcy baseline of 13.6±3.56, which drops to 10.7±2.81, which is maintained at 10.4±3.21 and 10.0 ±1.92 during the T3 and T4 time periods, where 1,800 mg NAC is administered to all groups. This supports a dose-dependent drop in the tHcy levels, which amounts to about 20-25% for

the highest dose (1,800 mg), compared to baseline (p. 111, 2nd paragraph), whereas the decrease in the Group B (600 mg dose) was about 10% (p. 110, 3rd paragraph. A linear interpolation of the percentage decrease predicts a 15-17.5% decrease is expected for 1200 mg dosage, but it is not clear what result would be expected for 1.2 mg dosed twice daily, because the Ventura study involved once daily dosing. The maximum expected decrease of tHcy for 2400 mg based on linear extrapolation (which ignores potential saturation behavior) would be 30-35%. These percentage decreases do not take into account any placebo effect.

Turning to the Friedman article, 1.2 g NAC was dosed twice a day to the individuals in the NAC arm of the clinical trial. Predialysis tHcy levels were reduced by a statistically significant amount of 19.2% (p. 444, last paragraph; Table 2), although the difference in the NAC and placebo group is not statistically significant, leading to the conclusion argued by applicant that tHcy levels were not significantly reduced by tHcy in hemodialysis patients (abstract). It is noted that the study was designed to detect a clinically significant difference of 25% with 80% power and a two-tailed alpha of 0.05 (pp. 443-444, bridging paragraph). The results show a trend toward modest tHcy-lowering effect in this treatment population (p. 445, 4th paragraph); the result was not statistically significant, on average the NAC patients had approximately 10% reduction in tHcy levels, with respect to placebo (p. 445, right, 2nd paragraph). It is noted that the article indicates that greater amounts of unbound homocysteine theoretically could be cleared by dialysis, but other studies did not find a dramatic decrease of tHcy levels after NAC therapy (p. 445, 6th paragraph); one pilot study found a 16% reduction in

predialysis levels 1.5-3 hours after oral NAC dose, and synergistic results were found with NAC therapy in conjunction with folate, but 500 mg/day did not significantly reduce postdialysis levels (p. 445, 6th paragraph).

Therefore, although "no effect" is the reported statistical result of the Friedman article, 10-19.2% is the amount considered to be determined by Friedman and is taken as the expected percentage reduction for NAC dosed at 1.2 g twice a day to individuals with ESRD. Compared to the amounts of 15-35%, which could be expected, based on Ventura in individuals with healthy kidneys, the amounts of Friedman are smaller than potentially expected. Comparing the two sets of values, leads to the calculated amounts of 1.5 to 1.82 greater reduction of tHcy by NAC in healthy patients over the ESRD patients. Considering that the Pendyala article indicates that at the highest dose levels of 7 and 8 g/m^2, thiols, including homocysteine, were reduced to 0-5% of the pretreatment levels in most patients (p. 1318, right, 2nd paragraph; Figure 2); i.e., 95-100% reduction is taught for tHcy in individals without ESRD. Applying the 1.5-1.82 reduction factor, discussed above, leads to an expectation of the range of 52-66% reduction of tHcy levels when the method of Pendyala is applied to individuals with ESRD. This reduction is comparable to that reported by applicant, for example, in Figure 3. Taking into consideration the uncertainty in the values reported by Ventura and Freidman, on which this prediction is based, the result reported by applicant is not considered surprising or unexpected, at least for the largest doses of Mesna rendered taught by Friedman. Therefore the disclosed results are not considered unexpected.

With respect to the removal of Mesna itself by dialysis, one of ordinary skill in the art would expect the removal of at least some of the Mesna, meeting the claim amendment limitation of “Mesna…[is]…removed from the plasma during dialysis” of claim 1. Considering Table 3 of Ventura, which indicates that 8.1-10.5% of the NAC is present as "free" NAC (fNAC); at a minimum, such “free” form of the compounds would be expected to be removed upon dialysis. Similar reduction in the free amount of Mesna would be expected for dialysis of an ESRD patient receiving Mesna accompanied by dialysis treatment.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Applicant further argues Johnson et al. (2002; “Dialysis of Drugs” chapter; IDS 2/23/2009 reference 34) states that the ability of mesna to be removed by dialysis was undetermined (p. 37); that the authors were not able to predict whether or not mesna could be removed by dialysis using information extrapolated from studies using conventional dialysis techniques, combined with the knowledge that mesna possesses certain undesirable side effects, which would be more serious in patients with ESRD, further supporting the unpredictability and non-obviousness of the presently claimed invention. With respect to the Johnson reference, the fact that the mesna dialysis

removal was not determined does not somehow render the obviated invention as unexpected. Removal of at least some mesna is expected as discussed above. The mesna remaining in the body would be primarily expected to be bound to a protein cysteine, such as bound to the plasma albumin. The levels of "free" mesna remaining unbound would be expected to be reduced by dialysis to levels below which side effects are significant. This is also supported by the Friedman study, which notes that noted side effects during the study were minimal (p. 445, 3rd paragraph).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1- are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites that Mesna is removed from the plasma during dialysis; however, for embodiments within the claims where Mesna is not administered, such as the administration of the Mesna derivative NAC, it is not clear what meaning removal of Mesna would have. It is assumed for the purposes of other rejections that the claim was intended to read that Mesna or the derivative thereof is removed from the plasma during dialysis.

It is also not clear what compounds are within the scope of “derivatives” of Mesna, and which are excluded.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3-5 and 7-14 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

While Mesna has been disclosed and is well known in the art, "derivatives" of mesna have not been disclosed to provide sufficient written description demonstrating applicant was in possession at the time of filing of the genus claim to “derivatives” of mesna, nor have a representative number of such derivative compounds been named or otherwise described.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> “To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a method of lowering elevated plasma total homocysteine levels in a subject with end stage renal disease comprising administering an effective amount of Mesna, or a derivative thereof, to a subject having end stage renal disease (ESRD) and performing dialysis on the subject wherein Hcy and Mesna re removed from the plasma during dialysis.

(1) Level of skill and knowledge in the art:

The level of skill and knowledge in the art are high.

(2) Partial structure:

The compound Mesna has been named. No partial structures that would be a required core structure of a "derivative" of Mesna have been disclosed.

(3) Physical and/or chemical properties and (4) Functional characteristics:

"Derivatives" of Mesna would have the claimed properties of lowering elevated tHcy levels in an ESRD subject subjected to dialysis, at least some compounds would presumably have a thiol group for exchange of Hcy on Hcy-cys34-albumin.

(5) Method of making the claimed invention:

No method of making any derivative of Mesna has been disclosed.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1, 3-5 and 7-14 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any compound which could somehow be viewed as a "derivative" of mesna. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of mesna and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984)

(affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102/103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 1, 3-5, 7-8 and 13-14 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Friedman et al. ("Te Effect of N-Acetylcysteine on Plasma Total Homocysteine Levels in Hemodialysis: A Randomized, Controlled Study"; 2003 Feb; American Journal of Kidney Diseases; 41(2): 442-446; IDS 2/23/2009 reference 15).

With respect to the removed Mesna during dialysis recited in the last two lines of claim 1, it is not clear what is meant by this phrase in as discussed above. For this rejection, it is assumed that the intention of the claim was the removal of mesna or the "derivative" of mesna that was administered from the plasma during dialysis.

Friedman teaches administration of N-Acetylcysteine (NAC) in patients undergoing hemodialysis (title); NAC was dosed orally at 1.2 g twice a day for 4 weeks (an effective amount; abstract); it is noted that in a paired analysis no statistically significant difference is reported between the NAC and placebo groups (abstract); however, tHcy levels are reported to have normalized on treatment (to ≤88.8 mg/L tHcy levels) for 3 of 16 patients (p. 445, 2nd paragraph); additionally Table 2 indicates an average 19.2% reduction in tHcy in all patients receiving NAC, which is reported to be significant result (i.e., NAC arm individuals had lowered tHcy levels; p. 444, last paragraph, Table 2); a high prevalence of cardiovascular risk factors is present in the chronic hemodialysis population, and homocysteine is among the putative risk factors (p. 442, 1st paragraph); NAC is a thiol-containing compound that has been found to acutely and dramatically reduce tHcy levels in healthy humans (p. 442, 3rd paragraph); hemodialysis patients would be undergoing dialysis on a regular schedule, such as three times weekly (daily administration for 4 weeks would involve dialysis subsequent to NAC administration); the trials involves human patients; standard vitamin supplements were administered, containing folic acid, Vitamin B6 and vitamin B12 (p. 443, 2nd paragraph); in an uncontrolled trial folic acid and oral NAC significantly reduced tHcy levels compared with either treatment alone (p. 442, 3rd paragraph). NAC would be a "derivative" of mesna, since it has activity in reduction of tHcy and has a reactive thiol group, like Mesna. It is noted that no mention is made of removal NAC from the plasma during dialysis. However, absent evidence to the contrary the mesna derivative NAC would be removed during dialysis as a characteristic of the method taught.

Additionally, reduction of cardiovascular risk and the risk of the specific diseases of claims 4 and 5 would characteristically accompany a 19.2% reduction of a recognized cardiovascular risk factor.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claim Rejections - 35 USC § 103

12. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman et al. (“Te Effect of N-Acetylcysteine on Plasma Total Homocysteine Levels in Hemodialysis: A Randomized, Controlled Study”; 2003 Feb; American Journal of Kidney Diseases; 41(2): 442-446; IDS 2/23/2009 reference 15) as applied to claims 1, 3-5, 7-8 and 13-14 above.

Friedman does not teach a weekly dose within any of the ranges of claims 9-12. However, Friedman teaches NAC supplementation in healthy subjects have been found to significantly reduce tHcy in a dose-dependent fashion within 1-2 hours (p. 445, 5th paragraph); a pilot study found a 16% reduction in predialysis tHcy levels 1.5-3 hours after an oral NAC dose. It would have been obvious to one of ordinary skill in the art at the time of the invention to optimize the dose, and timing of the dosing with respect to when the dialysis is conducted, which would have given amounts within the instant

claimed weekly and three times weekly amounts. The motivation would have been the routine optimization of conditions, and the minimal time exposure of a drug to maximize tHcy dialyzed while minimizing side effects of the drug therapy.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614